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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,087	04/11/2005	Sun Lee	3260-17	3610

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EXAMINER	
BAGGOT, BRENDAN O	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,087	LEE ET AL.	
	Examiner	Art Unit	
	Brendan O. Baggot	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction / Election

1. The Office acknowledges the receipt of Applicant's application, filed 4/11/05. Claims 1-8 are pending and examined in the instant application.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

2. Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

3. The abstract of the disclosure is objected to because of legalese: e.g., the word "comprising". Correction is required. See M.P.E.P. § 608.01(b).

Claim Objections

4. Claim 4 is objected to because of the following informalities: "NAA" should be defined in the claims before being used. Appropriate correction is required.

Claim Rejections - 35 U.S.C. §112, first paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for media set forth in the examples, does not reasonably provide enablement for medium having the ranges of plant growth regulators, plant cytokinins or inorganic compounds claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The *Wands* court set forth the enablement balancing test:

> Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *Wands* states at page 1404, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the 'claims."

See M.P.E.P. § 2164.01(a); See also *Ex Parte Forman* 230 USPQ 546, 547 (BdPatAppInt 1986); See also *Enzo Biochem, Inc., v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999).

"35 U.S.C. §112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. . . In cases involving. . .unpredictable factors. . .the scope of enablement. . .varies inversely with the degree of unpredictability. . ." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Applicant's claims are broadly drawn to a method of muskmelon (Cucumis melo., AKA cantaloupe or melon) cotyledon explant based transformation using media having a kinetin (6-furfurylamine) concentration of 3-8 mg/L, an IAA (indole-3-acetic acid) concentration of .5-3 mg/L, an NAA concentration of .08-.2 mg/L, an acetosyringone (4'-Hydroxy-3,5-dimethoxyacetophenone) concentration of 50-200μM or a Cu_2SO_4 concentration of .5-2 mg/L. Furthermore, claims 1-4 and 6 are broadly drawn to the use of any inoculation medium containing (or lacking) any hormone, growth regulator, inorganic salt or other addition.

Applicants teach a method of muskmelon (Cucumis melo., AKA cantaloupe or melon) cotyledon explant based transformation using inoculation and regeneration media having a kinetin (6-furfurylamine) concentration of 6 mg/L, an IAA (indole-3-acetic acid) concentration of 1.5 mg/L, and a Cu_2SO_4 concentration of .5-2 mg/L; wherein the inoculation medium additionally comprises an acetosyringone (4'-Hydroxy-3,5-dimethoxyacetophenone) concentration of 100μM.

Applicants do not teach a method of muskmelon (Cucumis melo., AKA cantaloupe or melon) cotyledon explant based transformation using media having a kinetin (6-furfurylamine) concentration of 3-8 mg/L, an IAA (indole-3-acetic acid)

concentration of .5-3 mg/L, an NAA concentration of .08-.2 mg/L, an acetosyringone (4'-Hydroxy-3,5-dimethoxyacetophenone) concentration of 50-200μM or a Cu_2SO_4 concentration of .5-2 mg/L. Furthermore, Applicants do not teach methods of muskmelon transformation using an inoculation medium which is free of acetosyringone and which contains cytokinins and auxins other than kinetin or IAA as recited in Claims 1-4 and 6.

The Nature of the Invention

The claims are drawn to methods and compositions relating to transgenic plants. The invention is in a class of inventions which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth Of The Claims

The claims are broadly drawn to and encompass melon transformation methods using plant growth regulators containing media having a kinetin concentration range of 3-8 mg/L, an IAA concentration range of .5-3 mg/L, an acetosyringone concentration range of 50-200μM and/or a Cu_2SO_4 concentration range of .5-2 mg/L.

The ratio of auxin to cytokinin in certain plant tissues is well known in the art to determine initiation of root versus shoot buds. Applicant's broad ranges encompass ratios of auxin to cytokinins which would not work and would produced undesired plant

growth. The broad language expressly includes cultured plant growth producing buds instead of the shoots desirable for plant transformation methods.

Quantity Of Experimentation

The quantity of experimentation in this area is large since melons have been known to be recalcitrant to transformation in the past, and because transformation of melon has been known to be poorly reproducible from one lab to the next and from one cultivar to the next. See the teachings Nuñez-Palenius and Rajagopalan discussed below. Also the relative levels of plant growth regulators are known to be important in the transformation method. The amount of experimentation necessary to solve the problems associated with reproducibility and transformation efficiency in muskmelon is very substantial, requiring extensive experimentation. This effort is an inventive, unpredictable and difficult undertaking in itself. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The Unpredictability of the Art and the State of the Prior Art

There is abundant prior art to suggest that transforming muskmelon is difficult, unpredictable and unsuccessful.

Even as late as 2006 Nuñez-Palenius teaches that ". . .*Cucumis melo* . . . has been recalcitrant to transformation by *Agrobacterium tumefaciens*. (2006) Journal Plant Cell Reports 25: 198-205, the abstract; *Id.* @ page 199, left column, 2nd parag.). Nuñez-Palenius also teaches that melon plants regenerated through plant tissue culture

methodologies are very susceptible to increases in ploidy levels when cultured *in vitro*. Unexpectedly, some leaves resulted in tetraploids. Nuñez-Palenius teaches that ethylene and gibberellins might have an important role in inducing increases in ploidy levels. Nuñez-Palenius continues that only 20% of the transgenic plants were diploid when cotyledon explants were used: cotyledon explants are a tissue with high propensity to bear tetraploid cells since the mature seed stage in cucurbits.(*Id.* @ 202).

Cürük concurs that melons are recalcitrant to transformation. (2005) Eng. Life Sci. 5(2) 169-177, *See* the title at least).

Rajagopalan, (2005) HortScience 40(2):431-435) teaches that "*Agrobacterium* mediated gene transfer is still far from routine in many recalcitrant species, including *Cucumis* [species]". (*Id.* @ page 431, left column, 2nd paragraph). As of the filing date of the application, it was even less predictable and more experimental than shown by Nuñez-Palenius, Cürük or by Rajagopalan.

Working Examples

The specification has no working examples of muskmelon (*Cucumis melo.*, AKA cantaloupe or melon) cotyledon explant based transformation using media with the broad ranges kinetin (6-furfurylamine) concentration of 3-8 mg/L, a IAA (indole-3-acetic acid) concentration of .5-3 mg/L, an acetosyringone (4'-Hydroxy-3,5-dimethoxyacetophenone) concentration of 50-200μM and/or a Cu_2SO_4 concentration of .5-2 mg/L.

Applicant does not teach working examples of the best auxin to cytokinin ratio in certain plant tissues to determine initiation of root versus shoot buds commensurate in scope with the ranges of plant growth regulators claimed.

Applicants do not teach working examples of successful muskmelon *Agrobacterium* mediated gene transfer using an inoculation medium which is free of acetosyringone, kinetin, or IAA in the inoculation medium or which contains cytokinins and auxins other than kinetin or IAA as recited in Claims 1-4 and 6.

Applicant does teach working examples of a kinetin (6-furfurylamine) concentration of 6 mg/L, an IAA (indole-3-acetic acid) concentration of 1.5 mg/L, an acetosyringone (4'-Hydroxy-3,5-dimethoxyacetophenone) concentration of 100μM and/or a Cu_2SO_4 concentration of 1 mg/L (Specification, Example 2-3).

Guidance in the Specification

The specification, while suggesting the use of a kinetin (6-furfurylamine) concentration of 6 mg/L, an IAA (indole-3-acetic acid) concentration of 1.5 mg/L, an acetosyringone (4'-Hydroxy-3,5-dimethoxyacetophenone) concentration of 100μM and/or a Cu_2SO_4 concentration of 1 mg/L, did not provide significant guidance on how to overcome art recognized problems in *Cucumis melo* transformation by Agrobacterium tumefaciens, how to determine the best ratio of auxin to cytokinin in certain plant tissues to cause initiation of root versus shoot buds, how to determine the factors affecting T-DNA delivery and subsequent plant regeneration, how to avoid abnormal somatic embryos or shoots, how to circumvent problems with reproducibility in transformation of

muskmelon, including muskmelon cultivar differences, or how to remedy the lack of reproducibility of transformation of *Cucumis melo* between different skilled artisans in different labs using the same method.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

In the instant case, along with the absence of working examples, the relatively small amount of guidance in the specification, the unpredictability in the art and the large amount of experimentation would be necessary to achieve function balanced only against the high skill level in the art, it is concluded that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Without sufficient guidance, determination of which combinations of growth regulators, and without guidance on how to overcome the deleterious effects of the wrong proportions of one regulator to others seen in transgenic plants, it is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. *See In re Wands*, 858 F.2d 731,8 USPQ2nd 1400 Fed. Cir, 1988)

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue trial and error experimentation would be required to practice the claimed

invention, and therefore the invention is not enabled throughout the broad scope of the claims.

Claim Rejections - 35 U.S.C. §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 U.S.C. §102(b).

6. Claims 1-3, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Bedbrook, et al., (5605011-US, Issued 25 February 1997). Bedbrook teaches (Bedbrook @ Example IX) a method for preparing a transformed *Cucumis melo*. (Bedbrook @ Example IX, particularly, col. 62, line 21), which comprises the steps of:(a) inoculating a cotyledon from *Cucumis melo* with *Agrobacterium tumefaciens* harboring a vector (Bedbrook @ Example IX, particularly, col. 62, line 35), in which the vector is capable of inserting into a genome of a cell from *Cucumis melo* and contains the following sequences: (i) a replication origin operable in the cell from *Cucumis melo*; (ii) a promoter capable of promoting a transcription in the cell from *Cucumis melo*; (iii) a structural gene operably linked to the promoter; and (iv) a polyadenylation signal sequence (*Id.* @ col. 66, line 6), (b) regenerating the inoculated cotyledon in a regeneration medium containing 3.0-8.0 mg/l of kinetin, including wherein an amount of kinetin in the regeneration medium of step (b) is 5.0-7.0 mg/l, (*Id.* @ col. 63, line 46-47), as growth regulator and 0.5-3.0 mg/l of IAA (Indole-3-acetic acid), including wherein an

amount of 1.0-2.0 IAA in the regeneration medium of step (b) is 1.0-2.0 mg/l, (*Id.* @ col. 63, line 46-47), and culturing the inoculated cotyledon to obtain regenerated shoots (*Id.* @ col. 62, line 48-49); and (c) culturing the regenerated shoots on a rooting medium (*Id.* @ col. 62, line 48-49) to obtain the transformed *Cucumis melo*.

"[I]noculating" reads upon dipping in infectious *Agrobacterium* (Bedbrook @ col. 62, line 35).

"[P]olyadenylation signal" reads upon a "transcription terminator" as taught by Bedbrook (col. 66, line 6).

As noted by the court in *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970), the notice of facts beyond the record which may be taken by the examiner must be "capable of such instant and unquestionable demonstration as to defy dispute" (citing *In re Knapp Monarch Co.*, 296 F.2d 230, 132 USPQ 6 (CCPA 1961)). MPEP § 2144.03.

Thus, the reference teaches all the limitations of the Claimed invention.

7. Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Bordas et al., 1997 Journal Transgenic Research 6, (1) pp. 41-50.

Claim 8 is drawn to a transformed muskmelon plant produced by a process comprising cuture of transformed cotyledon explants on a regeneration medium comprising kinetin as the cytokinin.

Bordas, et al., teaches a transformed muskmelon plant produced on a regeneration medium comprising benzyladenine as the cytokinin. (*See* page 42, column 1, bottom parag.).

The use of different cytokinin in the regeneration medium would not distinguish the transformed muskmelon plants taught by Bordas from the claimed transformed muskmelon.

In re Best teaches that where the prior art product seems to be identical to the claimed product, except that the prior art is silent as to a particularly claimed characteristic or property, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. *See In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

See In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985), which teaches that a product-by-process claim may be properly rejectable over prior art teaching the same product produced by a different process, if the process of making the product fails to distinguish the two products.

Thus, the reference teaches all the limitations of the Claimed invention.

Claim Rejections - 35 U.S.C. §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

> at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The *Graham* court set forth the factual inquiries that are applied for determining obviousness under 35 U.S.C. 103(a):

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being obvious over Bedbrook, et al., (5605011-US, Issued 25 February 1997) as applied to Claims 1-3 above and further in view of Bordas et al., (1997) Journal Transgenic Research 6, (1) pp. 41-50 and further in view of Sheikholeslam (1987) Plant Molecular Biology 8:291-298.

The teachings of Bedbrook have been discussed above.

Bedbrook does not teach the "regeneration medium" further comprising 0.5-2.0 mg/l of Cu2S04, 50-200 μM acetosyringone, or .08-0.2 mg/ml NAA.

Bordas teaches that 1mg/L Cu2SO4 enhances shoot regeneration in melon. (Bordas @ 42, left column, 5th paragraph). Bordas continues that growth regulators were replaced by [*either*] NAA or benzyladenine. Bordas also teaches 200 μM acetosyringone. (*Id.* @ page 42 left column, last paragraph, 45, left column, 2nd).

Sheikholeslam teaches that acetosyringone promotes high efficiency transformation of dicots. (*See* the title at least).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add 0.5-2.0 mg/l of Cu2S04, 50-200 μM acetosyringone, or .08-0.2 mg/ml NAA for the purposes of enhancing shoots regeneration as taught by Bordas. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success because the even the unskilled artisan would know that plants without roots won't grow. Also, Bordas specifically teaches NAA can replace IAA and that shoot regeneration was achieved only after the addition of acetosyringone.

Furthermore, it is well known in the art that 20μM acetosyringone in a non-melon species promotes high efficiency transformation of dicots. (Sheikholeslam (1987) Plant Molecular Biology 8:291-298, *See* the title at least).

The skilled artisan would recognize that transgenic calli don't grow without roots and therefore placing the calli on shooting media is a required intermediate step prior to

transferring to potting soil. Accordingly, one of ordinary skill in the art would have been motivated to generate the claimed invention with a reasonable expectation of success.

9. All Claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brendan O. Baggot whose telephone number is 571/272-5265. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571/272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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